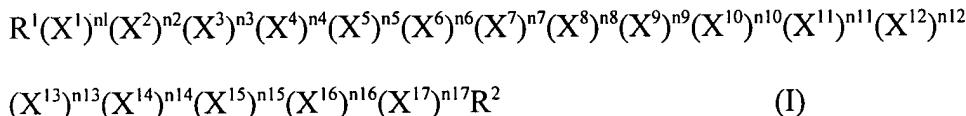


a.) Amendments to the Claims

1. (Currently Amended) A cyclic peptide, or a pharmaceutically acceptable salt thereof, having an activity to restore DNA-binding activity or P53 protein-dependent transcription activity to mutant P53 protein, said peptide being represented by formula (I):



wherein

any of X^1 to X^{17} may be denoted by X^i , i being an integer of 1 to 17;

any of $n1$ to $n17$ may be denoted by n_i , where n_i represents 0 or 1

such that $(X^i)^{n_i}$ represents X^i when n_i is 1 and represents a bond when n_i is 0;

~~ni represents 1 for at least 7 different X^i 's, with R^+ bonded to the N- terminus and R^2 bonded to the C-terminus: X^i 's;~~

any of X^1 to X^{11} where n_i represents 1 may be denoted by X^p , wherein p is 1-11 respectively, and any of X^8 to X^{17} where n_i represents 1 may be denoted by X^q where q is 8-17, respectively, such that $q > p$;

R^1 represents substituted or unsubstituted alkanoyl, substituted or unsubstituted alkoxy carbonyl, substituted or unsubstituted aralkyloxycarbonyl, substituted or unsubstituted aryloxycarbonyl, substituted or unsubstituted aroyl, 9-fluorenylmethoxycarbonyl or hydrogen;

R^2 represents substituted or unsubstituted alkoxy, substituted or unsubstituted aralkyloxy, amino, substituted or unsubstituted alkylamino, substituted or

unsubstituted dialkylamino, substituted or unsubstituted aralkylamino, substituted or unsubstituted arylamino or hydroxy;

~~R¹ and R² may together form a single bond when the total number of amino acid and organic acid residues having an SH group in the peptide is two or less, or a functional group in X^p and a functional group in X^q may together form a covalent bond to form a cyclic structure together with any intervening Xⁱ residues;~~

X¹ represents a residue of 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid, suberic acid, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-amino suberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline or 4-hydroxyproline;

X² represents a residue of leucine, isoleucine, valine, alanine, norvaline, norleucine, 2-aminobutanoic acid, homoleucine, β -alanine, α -aminoisobutanoic acid, β -cyclopropylalanine, β -chloroalanine, 1-aminocyclopentane-1-carboxylic acid, 1-amino-1-cyclohexanecarboxylic acid, 2-amino-1-cyclopentanecarboxylic acid, t-butylglycine, diethylglycine, t-butylalanine, O-methylserine, cyclohexylglycine, cyclohexylalanine or glycine;

X³ represents a residue of lysine arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X⁴ represents a residue of serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine,

aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-amino suberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X⁵ represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X⁶ represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X⁷ represents a residue of alanine, β -alanine, 2-aminobenzoic acid, 3-aminobenzoic acid, 4-aminobenzoic acid, 3-aminomethylbenzoic acid, proline, 3-hydroxyproline, 4-hydroxyproline, L-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid, cysteine, homocysteine, penicillamine, 2,3-diaminopropionic acid, 2,4-diaminobutanoic acid, ornithine, lysine, p-aminophenylalanine, aspartic acid, glutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-amino suberic acid or glycine;

X⁸ represents a residue of glutamine, asparagine, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-amino suberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, glycine, 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X^9 represents a residue of serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X^{10} represents a residue of serine, threonine, homoserine, α -methylserine, hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X^{11} represents a residue of serine, threonine, homoserine, α -methylserine, hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X^{12} represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X^{13} represents a residue of histidine, alanine, 4-thiazolylalanine, 2-

thienylalanine, 2-pyridylalanine, 3-pyridylalanine, 4-pyridylalanine, (3-N-methyl)piperidylalanine, 3-(2-quinoyl)alanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X^{14} represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic acid or glycine, and an amino group or guanidino group in the side chain of X^{14} may be modified with R^3 (where R^3 is independently selected from the moieties of R^1 ;

X^{15} represents lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X^{16} represents a residue of leucine, alanine, 4-thiazolylalanine, 2-thienylalanine, isoleucine, norleucine, homoleucine, valine, norvaline, β -alanine, α -aminoisobutanoic acid, 2-aminobutanoic acid, β -cyclopropylalanine, β -chloroalanine, 1-aminocyclopentane-1-carboxylic acid, 1-amino-l-cyclohexanecarboxylic acid, 2-amino-1-cyclopentanecarboxylic acid, t-butylglycine, diethylglycine, t-butylalanine, O-methylserine, cyclohexylglycine, cyclohexylalanine or glycine;

X^{17} represents a residue of 2-mercaptoaniline, cysteamine,

homocysteamine, cysteine, homocysteine, penicillamine, ornithine, lysine, 2,3-diaminopropionic acid, 2,4-diaminobutanoic acid, p-aminophenylalanine, glutamic acid, aspartic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid or 2-aminosuberic acid;

where a 12-aminododecanoic acid residue may be added at between R¹ and X^p nearest to the N- or C-terminus of the peptide N-terminus, or between X^q nearest to the C-terminus and R², and the cyclic peptide does not comprise five or more consecutive glycine residues.

2. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 1, wherein said cyclic structure is formed by a S-S, S-CH₂-S, S-CH₂-C₆H₄-CH₂-S, S-CH₂-CO, CO-NH, NH-CO, O-CO or CO-O bond between X^p and X^q.

3. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 2, wherein X^p (np=1) is an N-terminal residue and X^q (nq=1) is a C-terminal residue.

4. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 2, wherein X^p (np=1) is not an N-terminal residue and X^q (nq=1) is not a C-terminal residue.

5. (Previously Presented) A peptide or a pharmaceutically acceptable salt

thereof according to claim 2, wherein X^P ($np=1$) is not an N-terminal residue and X^q ($nq=1$) is a C-terminal residue.

6. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 2, wherein X^P ($np=1$) is an N-terminal residue and X^q ($nq=1$) is not a C-terminal residue.

7. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 3, wherein X^P ($np=1$) is X^1 and X^q ($nq=1$) is X^{17} .

8. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 6, wherein X^P ($np=1$) is X^1 and X^q ($nq=1$) is X^{17} .

9. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 3, wherein X^P ($np=1$) is X^1 and X^q ($nq=1$) is X^{16} .

10. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 6, wherein X^P ($np=1$) is an N-terminal residue and X^q ($nq=1$) is X^8 .

11. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 4, wherein X^P ($np=1$) is X^8 and X^q ($nq=1$) is X^{14} .

12. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 5, wherein X^P ($np=1$) is X^3 and X^q ($nq=1$) is a C-terminal residue.

13. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 4, wherein X^P ($np=1$) is X^3 and X^q ($nq=1$) is not a C-terminal residue.

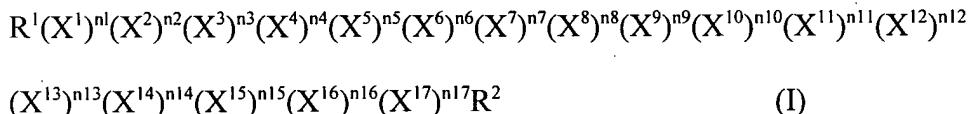
14. (Previously Presented) A peptide or a pharmaceutically acceptable salt thereof according to claim 6, wherein X^P ($np=1$) is an N-terminal residue and X^q ($nq=1$) is X^{11} .

15. (Currently Amended) A peptide or a pharmaceutically acceptable salt thereof according to claim 1, said peptide having an amino acid sequence shown by one of SEQ ID NOS: 4-7 and 16-32 in which a 12-aminododecanoic acid residue may be added between R^1 and X^P nearest to at the — or C- terminus of the peptide the N-terminus or between X^q nearest to the C-terminus and R^2 .

16. (Currently Amended) A peptide or a pharmaceutically acceptable salt thereof according to claim 15, said peptide having an amino acid sequence shown by one of SEQ ID NOS: 4-7, 16, 19 and 25-32 in which a 12-aminododecanoic acid residues may be substituted or added at the — or C- terminus of the peptide between R^1 and X^P nearest to the

N-terminus or between X^q nearest to the C-terminus and R².

17. (New) A cyclic peptide, or a pharmaceutically acceptable salt thereof, having an activity to restore DNA-binding activity or P53 protein-dependent transcription activity to mutant P53 protein, said peptide being represented by formula (I):



wherein

any of X¹ to X¹⁷ may be denoted by Xⁱ, i being an integer of 1 to 17;
any of n1 to n17 may be denoted by ni, where ni represents 0 or 1
such that (Xⁱ)ⁿⁱ represents Xⁱ when ni is 1 and represents a bond when ni is 0;
ni represents 1 for at least 7 different Xⁱs;
any of X¹ to X¹¹ where ni represents 1 may be denoted by X^p where p
is 1-11, respectively, and any of X⁸ to X¹⁷ where ni represents 1 may be denoted by X^q
where q is 8-17, respectively, such that q > p;

R¹ represents substituted or unsubstituted alkanoyl, substituted or
unsubstituted alkoxycarbonyl, substituted or unsubstituted aralkyloxycarbonyl, substituted
or unsubstituted aryloxycarbonyl, substituted or unsubstituted aroyl, 9-
fluorenylmethoxycarbonyl or hydrogen;

R² represents substituted or unsubstituted alkoxy, substituted or
unsubstituted aralkyloxy, amino, substituted or unsubstituted alkylamino, substituted or
unsubstituted dialkylamino, substituted or unsubstituted aralkylamino, substituted or

unsubstituted arylamino or hydroxy;

R^1 and R^2 together form a single bond;

X^1 represents a residue of 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid, suberic acid, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline or 4-hydroxyproline;

X^2 represents a residue of leucine, isoleucine, valine, alanine, norvaline, norleucine, 2-aminobutanoic acid, homoleucine, β -alanine, α -aminoisobutanoic acid, β -cyclopropylalanine, β -chloroalanine, 1-aminocyclopentane-1-carboxylic acid, 1-amino-1-cyclohexanecarboxylic acid, 2-amino-1-cyclopentanecarboxylic acid, t-butylglycine, diethylglycine, t-butylalanine, O-methylserine, cyclohexylglycine, cyclohexylalanine or glycine;

X^3 represents a residue of lysine arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X^4 represents a residue of serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid or

suberic acid;

X⁵ represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X⁶ represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X⁷ represents a residue of alanine, β-alanine, 2-aminobenzoic acid, 3-aminobenzoic acid, 4-aminobenzoic acid, 3-aminomethylbenzoic acid, proline, 3-hydroxyproline, 4-hydroxyproline, L-1,2,3,4-tetrahydroisoquinoline-7-carboxylic acid, cysteine, homocysteine, penicillamine, 2,3-diaminopropionic acid, 2,4-diaminobutanoic acid, ornithine, lysine, p-aminophenylalanine, aspartic acid, glutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic acid or glycine;

X⁸ represents a residue of glutamine, asparagine, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine, α-methylserine, 3-hydroxyproline, 4-hydroxyproline, glycine, 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X⁹ represents a residue of serine, threonine, homoserine, α-methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-

diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X^{10} represents a residue of serine, threonine, homoserine, α -methylserine, hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X^{11} represents a residue of serine, threonine, homoserine, α -methylserine, hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-aminosuberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, glycine, 2-mercaptopbenzoic acid, 3-mercaptopropionic acid, 4-mercaptopbutanoic acid, mercaptoacetic acid, adipic acid or suberic acid;

X^{12} represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X^{13} represents a residue of histidine, alanine, 4-thiazolylalanine, 2-thienylalanine, 2-pyridylalanine, 3-pyridylalanine, 4-pyridylalanine, (3-N-methyl)piperidylalanine, 3-(2-quinoyl)alanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-

amino adipic acid, 2-amino suberic acid, ornithine, lysine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X^{14} represents a residue of lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine, serine, threonine, homoserine, α -methylserine, 3-hydroxyproline, 4-hydroxyproline, cysteine, homocysteine, penicillamine, aspartic acid, glutamic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid, 2-amino suberic acid or glycine, and an amino group or guanidino group in the side chain of X^{14} may be modified with R^3 (where R^3 is independently selected from the moieties of R^1 ;

X^{15} represents lysine, arginine, ornithine, 2,4-diaminobutanoic acid, 2,3-diaminopropionic acid, p-aminophenylalanine or glycine;

X^{16} represents a residue of leucine, alanine, 4-thiazolylalanine, 2-thienylalanine, isoleucine, norleucine, homoleucine, valine, norvaline, β -alanine, α -aminoisobutanoic acid, 2-aminobutanoic acid, β -cyclopropylalanine, β -chloroalanine, 1-aminocyclopentane-1-carboxylic acid, 1-amino-l-cyclohexanecarboxylic acid, 2-amino-1-cyclopentanecarboxylic acid, t-butylglycine, diethylglycine, t-butylalanine, O-methylserine, cyclohexylglycine, cyclohexylalanine or glycine;

X^{17} represents a residue of 2-mercaptoaniline, cysteamine, homocysteamine, cysteine, homocysteine, penicillamine, ornithine, lysine, 2,3-diaminopropionic acid, 2,4-diaminobutanoic acid, p-aminophenylalanine, glutamic acid, aspartic acid, homoglutamic acid, isoaspartic acid, isoglutamic acid, 2-amino adipic acid or 2-amino suberic acid;

where a 12-aminododecanoic acid residue may be added between R¹
and X^p nearest to the N-terminus, or between X^q nearest to the C- terminus and R²,
and the cyclic peptide cannot be formed by cyclizing the peptides
represented by any of SEQ ID NOS: 33-41:

SEQ ID NO: 33: Arg Ala His Ser Ser His Leu Lys Ser Lys Lys
SEQ ID NO: 34: His Leu Lys Ser Lys Lys Gly Gln Ser Thr Ser
Arg His
SEQ ID NO: 35: Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu
SEQ ID NO: 36: Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys
Lys Leu
SEQ ID NO: 37: Arg Ala His Ser Ser His Leu Lys Ser Lys Lys
Gly Gln Ser Thr Ser Arg His Lys Lys
SEQ ID NO: 38: Ser His Leu Lys Ser Lys Lys Gly Gln Ser Thr
Ser Arg His Lys Lys Leu Met Phe Lys
SEQ ID NO: 39: Arg Ala His Ser Ser His Leu Lys Ser Lys Lys
Gly Gln Ser Thr Ser Arg His Lys Lys Leu Met
Phe Lys
SEQ ID NO: 40: Ser Arg Ala His Ser Ser His Leu Lys Ser Lys
Lys Gly Gln Ser Thr Ser Arg His Lys Lys Leu
Met Phe Lys
SEQ ID NO: 41: Gly Gly Ser Arg Ala His Ser Ser His Leu Lys
Ser Lys Lys Gly Gln Ser Thr Ser Arg His Lys
Lys Leu Met Phe Lys.